Monitoring International Trends

**posted September 2013**

The NBA monitors international developments that may influence the management of blood and blood products in Australia. Our focus is on:

* Potential new product developments and applications;
* Global regulatory and blood practice trends;
* Events that may have an impact on global supply, demand and pricing, such as changes in company structure, capacity, organisation and ownership; and
* Other emerging risks that could potentially put financial or other pressures on the Australian sector.

A selection of recent matters of interest appears below. Highlights include:

* The Committee for Medicinal Products for Human Use (CHMP) under the European Medicines Agency (EMA) recommended marketing authorisation for NovoNordisk’s recombinant factor VIII product turoctocog alfa (page 2).
* In the US a ten year old girl who received a cord blood transplant to treat sickle cell disease left hospital after three months with no sign of the disease at that time (Page 4).
* In the Netherlands, Sanquin reported that the demand for donated blood has decreased by 15 per cent over the last three years (Page 5).
* A case report in the [*Journal of Clinical Investigation*](http://www.jci.org/articles/view/66721) was described by a reviewer as providing the "first convincing evidence" for a direct donor contribution to a kidney recipient's skin squamous cell carcinoma (Page 5).
* Researchers have found the avian-origin H7N9 influenza A virus to be both virulent and easily-transmissible between humans (Page 9).
* Concern continues that Middle East Respiratory Syndrome (MERS) will be carried round the world by returning Hajj pilgrims (Page 10).

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# Products

*Here the NBA follows the progress in research and clinical trials that may within a reasonable timeframe make new products available, or may lead to new uses or changes in use for existing products.*

### Clotting factors

* 1. The Committee for Medicinal Products for Human Use (CHMP) under the European Medicines Agency (EMA) recommended marketing authorisation for NovoNordisk’s recombinant factor VIII product turoctocog alfa, with the intended brand name NovoEight, for the treatment and prophylaxis of bleeding in patients with haemophilia A. Novo Nordisk expects the final marketing authorisation from the European Commission within a few months and plans to launch NovoEight in Europe early in 2014. NovoEight has also been submitted for marketing authorisation in the US, Japan, Australia and Switzerland.

### Other

* 1. Daiichi Sankyo says its new blood clot preventer proved as effective as warfarin in treating venous thromboembolism and caused less bleeding. It said the drug appears to work best in sicker patients.
	2. [Octapharma USA](http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.octapharma.com&esheet=50699548&newsitemid=20130829005787&lan=en-US&anchor=Octapharma+USA&index=1&md5=c387ab3e4b16287219857dcfb98a8885) announced that [Octaplas](http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.octaplasus.com&esheet=50699548&newsitemid=20130829005787&lan=en-US&anchor=Octaplas%E2%84%A2&index=2&md5=7ef61bda423432f3a9799d4dea865edf) is available for ordering within the US. [Octaplas](http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.octaplasus.com&esheet=50699548&newsitemid=20130829005787&lan=en-US&anchor=Octaplas%E2%84%A2&index=3&md5=733dbaf120f3ee878d57226c27a81c62) is a solvent/detergent treated, pooled human plasma indicated for the replacement of multiple coagulation factors in patients with acquired deficiencies due to liver disease, or undergoing cardiac surgery or liver transplant, or for plasma exchange in thrombotic thrombocytopenic purpura.
	3. Grifols has announced the AlphaKit QuickScreen, a point-of-care device that can screen for alpha1-antitrypsin (AAT) deficiency. It is expected to be available for use in several European countries in early 2014.
	4. A new technique in cosmetic eyelid surgery uses fibrin glue instead of stitching. The glue consists of thrombin and fibrinogen, frozen as liquids, which are defrosted and mixed together before applying to a wound. The product triggers the clotting process and its proponents claim it reduces healing time.

# Regulatory

*The NBA monitors overseas regulatory decisions on products, processes or procedures which are or may be of relevance to its responsibilities.*

### Plasma and recombinant products

* 1. [CSL Behring](http://www.cslbehring.com/) received US Food and Drug Administration (FDA) approval for a 10 g (50 mL) vial size for Hizentra,Immune Globulin Subcutaneous (Human). This larger vial size will be available in the US in October.
	2. Cangene Europe Limited was granted a license to market WinRho 1500 LQ in Portugal for two indications: to prevent Rho(D) immunization in women who are Rho(D) negative, and to treat Rho(D) negative patients after incompatible Rho(D) positive blood transfusions or other products containing erythrocytes antigens.
	3. The FDA accepted Biomedica’s Investigational New Drug (IND) application for ClotFoam, a haemostat for intraoperative hemorrhage. Clinical trials will be supported by the National Heart Lung and Blood Institute of the US National Institutes of Health (NIH). Current trials are examining safety and efficacy as an adjunct in solid organ hemorrhage. Trials as a primary treatment in trauma patients could follow. ClotFoam relies on fast and powerful activity of fibrin monomer carried by foam with high affinity to endothelial tissue.

### Other

* 1. The EMA has granted orphan drug status**[[1]](#footnote-1)** in the European Union for Glycomimetics’ GMI-1070 in sickle cell disease. GMI-1070 has previously received both orphan drug and fast track status for from the FDA. It is being developed in partnership with Pfizer.
	2. The Australian Competition and Consumer Commission has decided not to oppose Baxter International's bid for Swedish dialysis product maker Gambro since Baxter plans to sell part of its unit that offers acute kidney failure treatments.
	3. In Germany the Federal Institute for Drugs and Medical Devices sees no new risks for patients using the clot-fighting Xarelto developed by [Bayer](http://www.fiercepharma.com/tags/bayer) and Johnson & Johnson. The agency was responding to a report in Der Spiegel that the number of side-effect reports and deaths in Xarelto patients had been growing. For the first 8 months of 2013, there were 968 side-effect reports, including 72 deaths, compared with 750 side-effect reports and 58 deaths during the whole of 2012.The use of Xarelto has been growing in both Europe and the US.

# Market structure and company news

*The NBA’s business intelligence follows company profitability, business forecasts, capital raisings or returns, mergers and takeovers, arrangements for joint research and/or development, contracts for supply of manufacturing inputs, and marketing agreements. Companies considered include suppliers, potential suppliers and developers of products which may be of interest.*

* 1. Biotest reported record sales for first half of 2013, with revenue up by 10.5 percent year on year, while profitability improved by a similar margin. Biotest's US division’s successful launch of Bivigam generated sales in the double-digit million range. The Board reaffirmed its target of increasing sales by ten to 15 per cent in the full year." Biotest is to expand its production capacity.
	2. [Cangene](http://www.genengnews.com/search?q=Cangene)’s [biodefense](http://www.genengnews.com/search?q=Biodefense) contract with the US Centers for Disease Control and Prevention ([CDC](http://www.genengnews.com/search?q=CDC)) was extended—just a year after an extension deal on contracts dating back to 2002.The new contract—under which the company supplies Vaccinia Immune Globulin Intravenous (VIGIV) into the US Strategic National Stockpile—was extended by 18 months, followed by three additional option periods to 2017. VIGIV is used to treat and prevent some complications from  [smallpox](http://www.genengnews.com/search?q=Smallpox) vaccination. The extension includes additional services to support license maintenance activities as well as options for additional manufacturing and plasma collections.
	3. Cangene has been awarded a five-year contract with the US Department of Health and Human Services (HHS), under which the company could be awarded delivery orders for the collection and storage of anti-anthrax human plasma, for the manufacturing of bulk drug substance and for Anthrax Immune Globulin Intravenous (AIGIV) the final drug product. Cangene's AIGIV, a hyperimmune antibody product specific for *Bacillus anthracis*, was first accepted into the US Strategic National Stockpile in 2007.
	4. Grifols announced the winners of the 2013 European Alpha1 Antitrypsin Laurell's Training Awards. The annual awards provide two fellowships of €50,000 to young investigators whose research contributes to the understanding and treatment of AAT deficiency. The 2013 recipients are Dr. Michael Emmet O'Brien of the Royal College of Surgeons in Ireland and Ms. Beata Poplawska of the National Institute of Tuberculosis and Lung Diseases in Poland. The awards were presented at the 2013 European Respiratory Society (ERS) Annual Congress in Barcelona.
	5. Plasma Technologies of North Carolina announced it had been granted a US patent #8,293,242, an "Ultra-High Yield of Alpha-1 Antitrypsin" and will commercialize its patented extraction process for plasma biologics. This significantly increases yield of AAT and intravenous immune globulin (IVIG) and allows the extraction of other therapeutic proteins. The company says “the non-denaturing process will enable plasma-derived biologics to be differentiated on the basis of improved molecular integrity that will enhance patient tolerance, will minimize the danger of thromboembolic events and will preserve the serum half-lives of the biomolecules”. The proprietary extraction process includes salt precipitation from plasma, with later salt removal by diafiltration. Final purification is by means of affinity and ion exchange chromatography.
	6. In the UK, the Nonwovens Innovation and Research Institute (NIRI) is partnering with Carbosynth[[2]](#footnote-2), Macopharma[[3]](#footnote-3) and NHS Blood and Transplant (NHSBT) in the Sanguis Project, which is being part-funded by the Technology Strategy Board. They hope to develop technology to remove blood group specific antibodies from donated blood, creating universal plasma.

# Country- specific events

*The NBA is interested in relevant safety issues which arise in particular countries, and also instances of good practice. We monitor health issues in countries from which Australia’*s *visitors and immigrants come.*

* 1. A ten year old girl at St. Louis Children’s Hospital was the third person to receive a cord blood transplant to treat sickle cell as part of a nationwide study involving Washington University School of Medicine; she left hospital after three months with no sign of the disease at that time.
	2. Regions Hospital, a level 1 trauma centre serving Minnesota and western Wisconsin, implemented strategies in 2011 to prevent red blood cell transfusions for patients who don’t need them and to ensure those who do get the right dose at the right time. Since then the average amount transfused monthly has dropped by 14 per cent.
	3. In the Netherlands, Sanquin reports that the demand for donated blood has decreased in the last three years by 15 per cent. Sanquin are closing 26 smaller collection sites.
	4. Northern Ireland’s most senior judge determined that a 28 year old Jehovah’s Witness with severe learning disabilities could be given blood against his mother’s wishes if his life were at risk during dental surgery. In Australia, a 17 year old Jehovah’s Witness has been judged by the NSW Court of Appeals not to be able to refuse a blood transfusion while being treated for Hodgkins lymphoma.
	5. In Jeddah, the Ministry of Health is preparing to fix the price of blood for transfusion to prevent exploitation by private hospitals.
	6. In New South Wales and Victoria, tranexamic acid will be available to paramedics for use to stem bleeding in trauma cases.

# Safety and patient blood management

*We follow current issues in patient safety and achieving favourable patient outcomes.*

### Treating iron deficiency

* 1. A new meta-analysis[[4]](#footnote-4) suggested that although intravenous iron may cut the need for blood transfusions, it comes with an increased risk of infections. The risk was contested[[5]](#footnote-5).
	2. Researchers from Imperial College London are developing technology for a portable finger-prick device to diagnose anaemia type quickly and on site. A paper authored by Dr Toby Basey-Fisher appeared in September in the journal Advanced Healthcare Materials. The team are currently patenting their technology and hope the product will be on the market within three years for use in accident and emergency wards, homecare and at the point of care for patients in developing countries.

### Other.

* 1. A case report in the [Journal of Clinical Investigation](http://www.jci.org/articles/view/66721) was described by a reviewer as providing the "first convincing evidence" for a direct donor contribution to a kidney recipient's skin squamous cell carcinoma.  Anne Janin of the University Caen Basse Normandie in Caen, France, and colleagues reported that skin tumour r cells with the donor genotype were found in the kidney recipient. The authors noted the potential clinical implications of prolonged immunosuppression.  They also pointed out that the long-term risk of complications for transplant recipients has increased, as more and more donors are older and as recipients live longer. Organ donor screening does not currently include testing for gene mutations.
	2. New research shows that use of antidepressants by pregnant women around their time of delivery increases their risk of postpartum haemorrhage[[6]](#footnote-6).
	3. Canadian Blood Services recalled 1,500 units of blood which were not properly tested for cytomegalovirus (CMV). CBS says that even though the test was not performed, the risks are low because white cells where CMV lies dormant are filtered from all donated blood.
	4. Review and meta-analysis suggested that “all oral anticoagulants and antiplatelet agents investigated ….were associated with a reduced recurrence of venous thromboembolism compared with placebo or observation, although acetylsalicylic acid was associated with the lowest risk reduction. Vitamin K antagonists given at a standard adjusted dose were associated with the greatest risk reduction in recurrent venous thromboembolism, but also the greatest risk of major bleeding”[[7]](#footnote-7).
	5. In a letter to healthcare professionals, Sanofi reported a small number of cases of acquired haemophilia in patients taking clopidogrel, despite having no prior history of abnormal coagulation.

# Research

*A wide range of scientific research has some potential to affect the use of blood and blood products. However, research projects have time horizons which vary from “useful tomorrow” to “at least ten years away”. Likelihood of success of particular projects varies, and even research which achieves its desired scientific outcomes may not lead to scaled-up production, clinical trials, regulatory approval and market development.*

* 1. Dr Kwaku Ohene-Frempong and colleagues at the Comprehensive Sickle Cell Center at Children’s Hospital of Philadelphia hope they may eventually be able to cure sickle cell disease through transplanting stem cells while babies are still in the womb.
	2. Doctors have not been able to track stem cells they implant to see if they take hold successfully. Now Stanford researchers have found that marking stem cells with the anemia drug ferumoxytol allows monitoring of the cells’ progress for four weeks through MRI scans.
	3. A study reported in the journal [*Pediatrics*](http://health/Pediatrics-What-is-Pediatrics.aspx)[[8]](#footnote-8) suggested that treating sickle cell anaemia with hydroxyurea reduced both hospitalization and annual estimated medical costs for infants and toddlers by 21 per cent.
	4. Scientists reported[[9]](#footnote-9) that they have identified the key molecule that stops adult cells from transforming into the induced pluripotent stem (iPS) cells that could be used to treat a variety of chronic diseases.
	5. A faster and simpler way to diagnose some blood infections has been developed by researchers at the University of Illinois, using the smell produced by the microbes. Results take 24 hours and do not require sophisticated equipment in a major laboratory. The new device starts with a hand-held plastic bottle filled with nutrient solution for bacteria to grow. Inside is a chemical sensing array with 36 pigment dots. These dots change colour in response to signature odours released by bacteria. The pattern of colour changes is unique to each strain of bacteria. The device, along with a desktop scanner and a computer, can identify eight of the most common disease-causing bacteria with almost 99 per cent accuracy[[10]](#footnote-10).
	6. [NovelMed](http://www.novelmed.com/) of Cleveland, Ohio is working with a humanized antibody that it hopes will block intra-and extra-vascular haemolysis[[11]](#footnote-11) in patients with paroxysmal nocturnal haemoglobinuria[[12]](#footnote-12) (PNH). The last improvement to treatment of PNH in the US was in 2007, when the FDA approved [Alexion Pharmaceuticals’ Soliris](http://www.alxn.com/solirisandpnh/default.aspx) which inhibits the destruction of red cells.
	7. A large study[[13]](#footnote-13) published online in the Journal of the American College of Cardiology reported that in heart transplants 31 per cent of blacks experienced graft failure compared with 27 per cent of Hispanics, 26 per cent of whites, and 21 per cent of Asians. The authors from Emory University School of Medicine in Atlanta suggested that multiple factors account for why African Americans have poorer survival and immunological differences may play a role.
	8. The long-term use of warfarin and consequent vitamin K deficiency has been found to have more implications than widely acknowledged, such as the calcification of organs that can lead to life-threatening problems like heart attack[[14]](#footnote-14).

# Legal actions and enquiries

*The NBA is interested in the implications for Australia of any proceedings against companies, governments and professional practitioners in relation to blood and blood products; or of relevant public enquiries.*

* 1. The European Court of Human Rights ruled that Italy must increase damages payments to people who were given HIV-tainted blood, to account for inflation.
	2. CSL and Baxter have been faced with a class action in the US which alleges the companies conspired to reduce the supply of immunoglobulin and albumin over a seven-year period. Reports say that CSL and Baxter requested that Dr Weinstein, an FDA official at the time of the alleged antitrust violations, testify; but that the FDA declined to allow Dr Weinstein to testify. Reports say CSL and Baxter then “moved to compel” the witness to testify and that the Court has agreed. In a recent financial statement release, CSL said: “The directors believe that future payment of a material amount in respect of litigation is remote. The Group has disclaimed liability for, and is vigorously defending, all current material claims and actions that have been made.”
	3. Baxter shareholders have been permitted by the US Court of Appeals for the Seventh Circuit to proceed with their lawsuit against the company’s directors over their management of issues concerning infusion pumps, and the subsequent FDA mandated recall.
	4. The UK Government has reversed a previous decision concerning the 2009-10 Pandemrix vaccine (for “swine flu”) and its possible causal link to narcolepsy. The Government said its review of fresh evidence has led it to accept that the vaccine could cause that condition. This renders the Government open to compensation claims.

# Infectious diseases

*The NBA takes an interest in infectious diseases because: the presence of disease in individual donors (e.g. influenza), or potential disease resulting from travel (e.g. malaria) means a donor must be deferred; temporary disease burden within a community (e.g. dengue in North Queensland) may limit blood collection in the community for a time; and some people may not be permitted to donate at all (e.g. people who lived in the UK for a period critical in the history of vCJD). Blood donations are tested for a number of diseases (e.g. HIV and Hepatitis B), but there are also emerging infectious diseases for which it may become necessary to test in the future (e.g. Chagas disease, and the tick-borne babesiosis and Lyme disease).*

### Mosquito- borne diseases: dengue, chikungunya and malaria

* 1. NanoViricides announced that an Orphan Drug Application has been submitted to the European Medicines Agency (EMA) for DengueCide, a drug candidate for the treatment of dengue and dengue haemorrhagic fever.
	2. Johnson & Johnson’s [Janssen](http://www.fiercebiotech.com/tags/janssen-0) unit has purchased global rights to compounds from a three-year alliance between the Rega Institute and the Centre for Drug Design and Discovery at KU Leuven. The compounds have been effective in animal tests in preventing replication of the [dengue virus](http://www.fiercebiotech.com/tags/dengue-fever-0).
	3. In Singapore, a "humanised mouse" has been developed to test dengue drugs.
	4. The ban on Townsville residents donating blood because of a dengue outbreak was lifted at the end of August.
	5. Scientists at the International Centre for Genetic Engineering and Biotechnology in New Delhi say they have developed a non-infectious dengue vaccine from yeast, and that animal trials of the vaccine have yielded satisfactory results. Dr Navin Khanna, group leader of the Recombinant Gene Products Group, said that "Efforts to develop a live attenuated vaccine (a vaccine created by reducing the virulence of a pathogen but still keeping it viable) have encountered unexpected interactions between the vaccine viruses, raising safety concerns. This underscored the need to experiment with non-replicating vaccine options." Partners in the project are the University of North Carolina School of Medicine and Ranbaxy research laboratories[[15]](#footnote-15).
	6. Two new tests have been developed which will help in tracking drug resistant malaria[[16]](#footnote-16).
	7. The West Australian Health Department announced that 31 Perth residents were diagnosed with Ross River virus (RRV) in the 4 weeks to 19 August, with a further 8 cases diagnosed outside the Perth area. A candidate RRV vaccine has been tested in humans. The adjuvanted, inactivated whole-virus Vero cell-derived vaccine is highly immunogenic in RRV-naive adults and well tolerated at all dose levels. This vaccine is not commercially available[[17]](#footnote-17).

### Influenza: strains, spread, prevention and treatment

* 1. A US study showed that pigs vaccinated against one flu strain were worse off if later infected with a related strain[[18]](#footnote-18).
	2. Sanofi announced its Fluzone High-Dose vaccine is more effective at preventing influenza in adults aged 65 and older than a standard dose of Fluzone.
	3. Visterra Inc. told the 53rd Interscience Conference on Antimicrobial Agents and Chemotherapy that its monoclonal antibody VIS410 can neutralize both the H5N1 and H7N9 strains of avian flu.
	4. A study has found that the avian-origin H7N9 influenza A virus attaches to the epithelium of both the upper and lower respiratory tracts. This has not previously been observed for other avian influenza A viruses[[19]](#footnote-19). Thijs Kuiken,of the department of viroscience at Erasmus University Medical Centre, said in a press release that “Abundant virus attachment to the human upper respiratory tract correlates with efficient transmissibility among humans.” This could lead to a pandemic. The virus causes severe pneumonia.
	5. Researchers at nine US sites began human testing of an H7N9 avian influenza vaccine. The two concurrent Phase II clinical trials were sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. A possible role for adjuvants is being examined.
	6. Japan says experts at the Health, Labor and Welfare Ministry will begin producing a vaccine for the H7N9 strain of avian influenza. The vaccine will be based on a strain produced by NIAID. The Ministry will test the vaccine on animals before deciding whether to conduct clinical trials on humans.

### MERS-CoV (Middle East respiratory syndrome, novel coronavirus)

* 1. The World Health Organization announced on 7 September that MERS virus has led to 144 infected cases and 54 deaths. Most cases had been in Saudi Arabia.
	2. An analysis suggests the virus first appeared in animals about July 2011 and multiple infections of people followed. The virus was then transmitted by people to people[[20]](#footnote-20).
	3. Cochin International Airport decided to implement precautionary measures against MERS CoV. The Middle East is the source of most international traffic to the airport.
	4. The first known MERS death in the United Arab Emirates occurred at the end of August 2013,
	5. Writing in Nature Medicine on September 8, a team led by researchers at NIAID offered a therapeutic approach to MERS validated in nonhuman primates. Darryl Falzarano and his colleagues showed in a rhesus macaque model that treatment with interferon-α2b and the nucleoside inhibitor ribavirin improved clinical outcome when administered eight hours post-infection[[21]](#footnote-21).
	6. Indonesia’s Hajj pilgrims began departing for Saudi Arabia. 168,800 pilgrims will make the journey from Indonesia this year. Groups travel to Saudi Arabia between 10 September and 9 October. They will return to Indonesia between 19 October and 4 November, and it is widely expected that some will return with MERS. Indonesia’s health ministry is preparing thermal scanners for returning pilgrims in the hope of slowing the spread of the virus.

### Other diseases: occurrence, prevention and treatment

* 1. University of Hong Kong microbiologist Yuen Kwok-yung advised that H7N9 bird flu may be spreading through human faeces, as researchers found the virus in the stools of 4 out of 6 people who died in Zhejiang. In Kowloon during the 2003 SARS outbreak the virus spread through sewage pipes. Yuen emphasised the implications of the discovery for infection control strategies[[22]](#footnote-22).
	2. Queensland Health was notified of six measles cases in the month to September 6 and was concerned about the potential spread of the virus. By 11 September the NSW North Coast Public Health Unit was advising a Tweed area alert.
	3. The CDC considered over a decade's worth of data on measles cases to the end of August 2013 and found that most patients had not been vaccinated. The report concluded that although the US declared measles eliminated nationally in 2000, anti-vaccination believers were causing a return of the disease.
	4. Jean-Pierre Zellweger, of the University of Lausanne, and colleagues reported at the [European Respiratory Society meeting](http://www.erscongress2013.org/) on their tracing study of tuberculosis-exposed people. They confirmed the accepted wisdom that close family contacts of tuberculosis were more likely to acquire the disease than other contacts.
	5. Theraclone Science announced it had dosed the first patient in a Phase IIa trial of TCN-202 for the prevention of human CMV infection in solid organ transplant recipients.
	6. In the US, insufficient sterilization of instruments at a New Hampshire hospital has led to concerns about a possible “outbreak” of Creutzfeld-Jacob disease.
	7. Scientists from [Curtin University](http://www.curtin.edu.au/) and [The University of Western Australia](http://www.uwa.edu.au/) are hoping to develop a new whooping cough vaccine to be delivered via nasal spray. They say the vaccine should be more effective than current vaccines, have fewer side effects, offer long- term protection and require fewer booster doses. They hope it will be commercially available within five to eight years[[23]](#footnote-23).
1. Orphan drug designation in the EU is granted for products to diagnose, prevent or treat rare diseases that are life-threatening or very serious. A disease is “rare” in the EU if it affects fewer than five in 10,000 people. In the EU the designation offers a 10-year period of market exclusivity, access to a centralized review process, protocol assistance and scientific advice, waiving or reduction of certain fees, and eligibility for grants and R&D support. [↑](#footnote-ref-1)
2. Carbosynth is a specialist in carbohydrates and nucleosides for the pharmaceutical and biotech communities. [↑](#footnote-ref-2)
3. Macopharma is experienced in transfusion, infusion and bioengineering. [↑](#footnote-ref-3)
4. Published online August 15 in *BMJ.* Lead author Dr Edward Litton of the University of Western Australia. [↑](#footnote-ref-4)
5. Dr Michael Auerbach of Georgetown University in Washington, DC, told Reuters Health that any increase in infections with IV iron "is vanishingly small." [↑](#footnote-ref-5)
6. Kristin Palmsten et al., “Use of antidepressants near delivery and risk of postpartum hemorrhage: cohort study of low income women in the United States”, *BMJ* 2013;347:f4877 doi: 10.1136/bmj.f4877 (Published online 21 August 2013) [↑](#footnote-ref-6)
7. Lana A Castellucci, et al, “Efficacy and safety outcomes of oral anticoagulants and antiplatelet drugs in the secondary prevention of venous thromboembolism: systematic review and network meta-analysis”, *BMJ* 2013; 347:f5133 doi: <http://dx.doi.org/10.1136/bmj.f5133> (Published 30 August 2013) [↑](#footnote-ref-7)
8. Principal investigator was Winifred Wang of the Department of Hematology at St. Jude Children's Research Hospital. [↑](#footnote-ref-8)
9. September 18 online, in *Nature.* Principal investigator: Jacob Hanna, Laboratory for Pluripotent Cell Studies, Weizmann Institute of Science, Rehovot, Israel. [↑](#footnote-ref-9)
10. The study was reported at the 246th National Meeting and Exposition of the American Chemical Society. [↑](#footnote-ref-10)
11. Haemolysis is the rupturing of red blood cells and the release of their contents into surrounding fluid such as [blood plasma](http://en.wikipedia.org/wiki/Blood_plasma). [↑](#footnote-ref-11)
12. PNH causes part of the immune system to kill red blood cells, which leads to fatigue, weakness, pale skin, shortness of breath, abnormal blood clotting and red urine. [↑](#footnote-ref-12)
13. [Morris AA, et al "Influence of race/ethnic differences in pre-transplant panel reactive antibody of outcomes in heart transplant recipients" *J Am Coll Cardiol* 2013; DOI: 10.1016/j.jacc.2013.06.054.](http://content.onlinejacc.org/article.aspx?articleID=1732384) Also [Pinney SP, "Understanding and eliminating racial disparities in transplantation: still a ways to go" J Am Coll Cardiol 2013; DOI:10.1016/j.jacc.2013.07.070.](http://content.onlinejacc.org/article.aspx?articleid=1732397) [↑](#footnote-ref-13)
14. Monash University’s Emeritus Professor Wahlqvist, former head of medicine at the Monash Medical Centre, and collaborators reviewed a case of calcification of the coronary artery in a patient after a decade on warfarin; and their review reverberated quickly round the world. [↑](#footnote-ref-14)
15. The research has been published in the journal, *PLOS One.* [↑](#footnote-ref-15)
16. **Witkowski B, Amaratunga C, Khim N, et al.** “Novel phenotypic assays for the detection of artemisinin-resistant Plasmodium falciparum malaria in Cambodia: in-vitro and ex-vivo drug-response studies”. *Lancet Infect Dis* 2013 Sep 11 and **Sibley CH.** “Tracking artemisinin resistance in Plasmodium falciparum”. (Editorial) *Lancet Infect Dis* 2013 Sep 11. [↑](#footnote-ref-16)
17. Aichinger G, Ehrlich HJ, Aaskov JG, Fritsch S, Thomasser C, Draxler W, Wolzt M, Müller M, Pinl F, Van Damme P, Hens A, Levy J, Portsmouth D, Holzer G, Kistner O, Kreil TR, Barrett PN. “Safety and immunogenicity of an inactivated whole virus Vero cell-derived Ross River virus vaccine: a randomized trial”. 2011. *Vaccine* 29(50):9376-84. [↑](#footnote-ref-17)
18. Dr Hana Golding of the Center for Biologics Evaluation and Research at Bethesda in Maryland and colleagues at the National Animal Disease Center published their report in *Science Translational Medicine*. “Vaccine-Induced Anti-HA2 Antibodies Promote Virus Fusion and Enhance Influenza Virus Respiratory Disease”, *Sci Transl Med* 28 August 2013: Vol. 5, Issue 200, p. 200ra114 Sci. Transl. Med. [DOI: 10.1126/scitranslmed.3006366](http://dx.doi.org/10.1126/scitranslmed.3006366).  They cautioned that their results may not apply to humans, and that the vaccines they used were made from whole, killed viruses. Those used in humans are made from parts of killed viruses. [↑](#footnote-ref-18)
19. The report was published in the October 2013 issue of *The American Journal of Pathology*. See also Y Yi Shi et al, “Structures and Receptor Binding of Hemagglutinins from Human-Infecting H7N9 Influenza Viruses. *Science* DOI: 10.1126/science.1242917 <<http://www.sciencemag.org/content/early/2013/09/04/science.1242917> [↑](#footnote-ref-19)
20. Reported in *The Lancet*, 20 September [↑](#footnote-ref-20)
21. **D. Falzarano et al., “Interferon-α2b and ribavirin treatment improves outcome in MERS-CoV-infected rhesus macaques,”** Nature Medicine**, doi: 10.1038/nm.3362, 2013.** [↑](#footnote-ref-21)
22. *Clinical Infectious Diseases*, 13 August 2013. [↑](#footnote-ref-22)
23. After an intensive vaccination campaign, the number of cases in Australia dropped from 38,500 in 2011 to 26,000 in 2012, but this is high for a preventable infectious disease which is potentially fatal in babies. [↑](#footnote-ref-23)